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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,670	03/12/2001	Wei Shao	CL000524	8111

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/803,670	Applicant(s) SHAO ET AL.	
	Examiner Sandra Wegert	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8,9 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's election without traverse of Invention III, (claims 4, 5, 8-11, 22, and 23) in Paper No. 9 (29 January 2002) is acknowledged. In addition, Applicant elected the following: The nucleotide(s) encoding the polypeptide of SEQ ID NO: 2. In Paper No. 9, claims 1-3, 6-7, and 10-23 were cancelled by the Applicant; Claims 24-29 were added and read on the elected invention.

Claims 4, 8, 9 and 24-29 are under examination in the current application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "NUCLEIC ACIDS ENCODING A HUMAN TRANSPORTER PROTEIN".

Appropriate correction is requested.

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, on page 5, line 7. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 4, 8, 9 and 24-29 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to polynucleotides and the recombinant expression of the peptide of SEQ ID NO: 2. The specification asserts that the claimed polynucleotides encode a novel *sulfate transporter* protein.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the claimed polynucleotide and the polynucleotides and recombinant methods used to express the disclosed polypeptide:

1) To produce or search for a variant or chimeric nucleotide or polypeptide,

2) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide,

3) For the production of antibodies,

4) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 2 and to localize gene expression in tissue samples,

5) In the creation of transgenic animals,

6) To detect pharmacogenomically-relevant polymorphisms in individuals,

7) For gene therapy.

Each of these shall be addressed in turn:

1) To produce or search for a variant or chimeric nucleotide or polypeptide. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Furthermore, the specification discloses nothing specific or substantial for the

variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide. This asserted utility is credible and specific. However, it is not substantial. The specification does not characterize the polypeptide encoded by the polynucleotide of the claimed invention. Therefore binding sites, etc. are not identified. Significant further experimentation would be required of the skilled artisan to characterize the protein and search for ligands. There is no disclosure, for example, of how to assay for ligand binding and possible transduction mechanisms. It is not known the class of drugs to use or what measurements to perform. Since this asserted utility is not presented in mature form so it could be readily used in a real world sense, the asserted utility is not substantial.

3) For the production of antibodies. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

4) To make hybridization probes and primers to detect nucleic acid molecules that encode the polypeptide of SEQ ID NO: 2 and to localize gene expression in tissue samples. This asserted utility is credible but not substantial or specific. Hybridization probes and primers can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) In the creation of transgenic animals. This asserted utility is credible but not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the present invention. Significant further experimentation would be required of the skilled artisan to identify such a disease. The specification discloses nothing about whether the claimed gene will be "knocked in" or "knocked out" or what specific tissues and cells are being targeted. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6) To detect pharmacogenomically-relevant polymorphisms in individuals. This asserted utility may be credible, however it is neither specific nor substantial. There are many examples where polymorphisms have been adequately described in clinically relevant genes. As an example, there are several important polymorphisms that occur in metabolic enzymes (e.g. the liver P450's or the dehydrogenases) that are very well characterized physiologically and within populations. Applicants have not demonstrated the function of the polypeptide encoded by the claimed polynucleotide, and have not identified clinically relevant polymorphisms. Therefore, the asserted utility is not substantial. Finally, many unrelated sequences can be polymorphic, generally. Thus, the asserted utility is not specific.

7) For gene therapy. This asserted utility is credible but not specific or substantial. Such can be performed for any polynucleotide. Further, the specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the claimed invention. Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease and to determine the route of administration of the gene, as well as quantity and

duration of treatment. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Claims 4, 8, 9 and 24-29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 4, 8, 9 and 24-29 are directed to isolated nucleic acid molecules that encode a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. The claims also recite a nucleic acid molecule that has a nucleotide sequence comprising the nucleotides of SEQ ID NO: 1. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the polypeptide having the amino acid sequence of SEQ ID NO: 2, a recombinant host cell, a nucleotide that hybridizes to the polynucleotide of SEQ ID NO: 1, and a process of producing a recombinant host cell and polypeptide.

The specification teaches the polynucleotides encoding the polypeptide of SEQ ID NO: 2, and asserts the polypeptide is a new sulfate transporter. However, the specification does not teach functional or structural characteristics of the polynucleotide or polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the

specific details of protein function (see Box 2, p. 36). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity.

Bisson, *et al* (1993, Crit Rev Biochem Mol Biol, 28:259) studied yeast transporter knockout phenotypes, and found little correlation between homology and the substrate transported. For example, they found that yeast transporters *Gal2* and *Hxt4* displayed 83.7% homology, but *Gal2* appears to transport Galactose, while *Hxt4* appears to transport Glucose (based on knockout phenotype- compare Table 1 and Table 2A). Similarly, Liang et al found that several single amino acid substitutions in yeast glucose transporters can change substrate specificity (Liang, H., et al (1998) Mol. Cell. Biol. 18(2): 926).

Based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make biologically active polypeptide without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding the polypeptide for *any* purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polynucleotides encoding the polypeptide could be used as a diagnostic tool.

There is no data on the substrates transported by the polypeptide of the Instant Specification, nor on phenotypic changes in cells transfected with the polynucleotides of the Instant Invention. The lack of disclosed functional examples means that the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any unique purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide, such that it can be determined how to use the claimed polynucleotides encoding the polypeptide of SEQ ID NO:2 and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, second paragraph-indefiniteness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claim 24 is rendered indefinite because the specification does not teach how to recombinantly produce a polypeptide from the complementary nucleic acid (refer to claim 4(d)).

Conclusion: Claims 4, 8, 9 and 24-29 are rejected for the reasons listed above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

11/21/02

ELIZABETH [illegible]
PRIMARY EXAMINER